Amendments to the Specification

Please replace the paragraph beginning on page 19, line 11 with the following amended paragraph:

An affinity threshold associated with immunogenicity in the context of HLA class II DR molecules has also been delineated (*see, e.g.*, Southwood *et al. J. Immunology* 160:3363-3373, 1998, and co-pending U.S.S.N. 09/009,953 filed 1/21/98, now U.S. Patent No. 6,413,517). In order to define a biologically significant threshold of DR binding affinity, a database of the binding affinities of 32 DR-restricted epitopes for their restricting element (*i.e.*, the HLA molecule that binds the motif) was compiled. In approximately half of the cases (15 of 32 epitopes), DR restriction was associated with high binding affinities, *i.e.* binding affinity values of 100 nM or less. In the other half of the cases (16 of 32), DR restriction was associated with intermediate affinity (binding affinity values in the 100-1000 nM range). In only one of 32 cases was DR restriction associated with an IC_{50} of 1000 nM or greater. Thus, 1000 nM can be defined as an affinity threshold associated with immunogenicity in the context of DR molecules.

Please replace the paragraph beginning on page 32, line 26 with the following amended paragraph:

Although peptides with suitable cross-reactivity among all alleles of a superfamily are identified by the screening procedures described above, cross-reactivity is not always as complete as possible, and in certain cases procedures to increase cross-reactivity of peptides can be useful; moreover, such procedures can also be used to modify other properties of the peptides such as binding affinity or peptide stability.

Having established the general rules that govern cross-reactivity of peptides for HLA alleles with a given motif or supermotif, modification (*i.e.*, analoging) of the structure of peptides of particular interest in order to achieve broader (or otherwise modified) HLA binding capacity can be performed. More specifically, peptides which exhibit the broadest cross-reactivity patterns, can be produced in accordance with the teachings herein. The present concepts related to analog generation are set forth in greater detail in co-pending U.S.S.N. 09/226,775 filed 1/6/99, now abandoned.

Please replace the paragraph beginning on page 50, line 17 with the following amended paragraph:

For instance, the ability of a peptide to induce CTL activity can be enhanced by linking the peptide to a sequence which contains at least one epitope that is capable of inducing a T helper cell response. The use of T helper epitopes in conjunction with CTL epitopes to enhance immunogenicity is illustrated, for example, in the co-pending applications U.S.S.N. 08/820,360, now abandoned; U.S.S.N. 08/197,484, now U.S. Patent No. 6,419,931; and U.S.S.N. 08/464,234, now abandoned.

Please replace the paragraph beginning on page 68, line 24 with the following amended paragraph:

Peptide engineering strategies were implemented to further increase the cross-reactivity of the epitopes identified above. On the basis of the data enclosed, *e.g.*, in related and co-pending U.S.S.N. 09/226,775, now abandoned, the main anchors of A2-

supermotif-bearing peptides are altered, for example, to introduce a preferred L, I, V, or M at position 2, and I or V at the C-terminus.

Please replace the paragraph beginning on page 78, line 16 with the following amended paragraph:

This example provides general guidance for the construction of a minigene expression plasmid. Minigene plasmids may, of course, contain various configurations of CTL and/or HTL epitopes or epitope analogs as described herein. Expression plasmids have been constructed and evaluated as described, for example, in co-pending U.S.S.N. 09/311,784 filed 5/13/99, now U.S. Patent No. 6,534,482.

Please replace the paragraph beginning on page 79, line 31 with the following amended paragraph:

The degree to which the plasmid construct prepared using the methodology outlined in Example 11 is able to induce immunogenicity is evaluated through *in vivo* injections into mice and subsequent *in vitro* assessment of CTL and HTL activity, which are analyzed using cytotoxicity and proliferation assays, respectively, as detailed *e.g.*, in U.S.S.N. 09/311,784 filed 5/13/99, now U.S. Patent No. 6,534,482 and Alexander *et al.*, *Immunity* 1:751-761, 1994.